

REMARKS

With the entry of the amendments above, claims 1, 3-8 and 10-33 are pending in the application.

Claims 2 and 9 are canceled above without prejudice or disclaimer. The limitations of claims 2 and 9 have been added to claim 1 (with correction of the spelling of the compound "thioguanine," which was misspelled in original claim 9 as "thiogaunine"). Three Markush elements (platinum complexes, carboplatin, and cisplatin) are removed from the Markush group as it appeared in original claim 9. The term "crystalline forms" is deleted from claim 1. The term "onium reagents" in claim 18 has been amended to "uronium and phosphonium reagents" (with support at paragraph 0048, pages 18-19) This amendment simply replaces the term "onium" with more commonly used terms, and is not a narrowing amendment. The term "compound" has been changed to "composition" in the claims. New claims 19-33 are added in this amendment. These claims are supported by original claims 12, 13, 14, and 15, and by the specification at pages 23-25, paragraphs 0056 and 0057, and page 28, paragraph 0067. No new matter is added by this amendment.

With respect to any claim amendments or cancellations, Applicants have not dedicated to the public or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Information Disclosure Statement

An Information Disclosure Statement is enclosed with this response. Applicants respectfully request that the Examiner consider the references submitted and make them of record in the application, and return the initialed Form SB/08.

Rejection Under 35 USC § 112, First Paragraph

Claims 1-11 and 13-18 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for making and using a porphyrin and a chemotherapeutic covalently linked with a group other than –NH-C(O)-(CH₂)₂.

Applicants thank the Examiner for the extensive discussion of the claims in view of the *Wands* factors. However, Applicants respectfully traverse this rejection. While Applicants submit that the previously pending claims were fully enabled, the claims have been amended to expedite prosecution. The *Wands* factors are thus discussed as they might apply to the amended claims.

Regarding factor 1, the breadth of the claims has been changed, by the recitation of the limitations of original claim 9 in currently amended claim 1. These compounds are known classes of chemotherapeutic agents; the amended claims are directed to compounds and classes of compounds known to be effective in cancer treatment.

Regarding factor 2, the nature of the invention, the Examiner states that cancer therapeutics are highly unpredictable. However, it should be noted that the classes of compounds recited in currently amended claim 1 are known classes of chemotherapeutic compounds. The Applicants have demonstrated that conjugation to a porphyrin decreased the toxicity of doxorubicin, while preserving the anti-cancer effect of doxorubicin (see the specification at page 30, paragraph 0072).

Regarding factor 3, the state of the prior art, the Examiner states that the "...showing of a single compound does not provide [an] adequate representation to enable one to synthesize porphyrins linked to a vast number of chemotherapeutic compounds..." However, the specification provides additional guidance on linking of porphyrins to polyamines. Paragraph 0048 at pages 18-19 discusses chemical agents that can be used to condense carboxylic-acid containing porphyrins with chemotherapeutic agents containing an amino group or a hydroxy group. Paragraph 0049 at pages 19-20 discusses cross-linking chemistry which can be used for the compounds of interest. Paragraph 0050 at page 20 discusses methods of derivatizing porphyrins, such as etioporphyrin, which lack a readily-activatable group.

Regarding factor 5, the Examiner states that the synthesis of porphyrin compounds is unpredictable and difficult. However, the porphyrin compounds described for use in the invention have already been synthesized; thus there is no unpredictability involved. The linkage of porphyrin compounds to chemotherapeutic agents is discussed at pages 18-20 (paragraphs 0048-0050). In light of the fact that the claims as amended recite known classes of chemotherapeutic agents, the lack of interchangeability of chemotherapeutic agents for treating uncontrolled cell proliferation is moot to the predictability of the known types of chemotherapeutic agents recited.

Regarding factor 6, the invention provides a reasonable amount of guidance to the skilled artisan, in that chemical groups on the porphyrins are described which can be reacted with chemical groups on the chemotherapeutic agents (paragraph 0048, pages 18-19). Procedures for derivitization of non-reactive porphyrins are also provided (paragraph 0050, page 20).

Regarding factors 7 and 8 (working examples and quantity of experimentation), it is submitted that, in view of the guidance provided in the sections cited above (paragraphs 0048-0050, pages 18-20) and in the examples (paragraphs 0058-0072, page 25-30), the skilled artisan would be able to practice the invention across the scope of the claims without undue experimentation.

In view of the comments above, reconsideration and withdrawal of the rejection under 35 USC § 112, first paragraph is respectfully requested.

Rejection Under 35 USC § 112, Second Paragraph

Claims 1-18 were rejected under 35 USC § 112, second paragraph as allegedly being indefinite.

This rejection is respectfully traversed. Applicants submit that the claims as originally presented were not indefinite. However, the claims have been amended to expedite prosecution. One of skill in the art will recognize the meaning of “chemotherapeutic agents,” and the skilled artisan can clearly identify whether a compound falls within the classes of chemotherapeutics listed. The skilled artisan can clearly recognize a porphyrin moiety. And the skilled artisan can clearly

recognize a covalent bond or covalent linking group between a porphyrin and a chemotherapeutic agent. Accordingly, the metes and bounds of the claims are clear and definite.

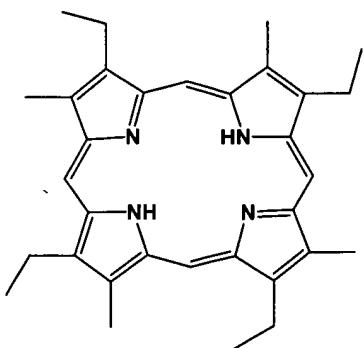
The Examiner objected to the term “crystalline forms.” While Applicants do not agree that this term is indefinite, it has been removed from the claim in order to expedite prosecution. Applicants submit that this is not a narrowing amendment, that is, removing the term “cystalline forms” does not change the scope of the claim, since the claim still necessarily embraces all crystalline and non-crystalline forms of the compound. The rejection is thus moot with respect to the term “crystalline forms,” and withdrawal of the rejection is respectfully requested.

The Examiner also stated that the location of the covalent linking group was not identified. It is not apparent how the claims are indefinite, since one of skill in the art would readily recognize a moiety which links two individual components of a compound. Applicants submit, in view of the identification of the various functional groups that can be utilized for covalent coupling in the specification (see, e.g., paragraphs 0048-0050, at pages 18-20), and the description of the cross-linking chemistry in the cited reference Wong in paragraph 0049, that the location of the linking group need not be specified for the claims to be definite. Accordingly, withdrawal of these rejections under 35 USC § 112, second paragraph, along with withdrawal of the rejections of claims 3, 7, 8, 10, 11, 12, 14, 17 and 18 for dependence on an indefinite claim, is respectfully requested.

Rejection Under 35 USC § 102

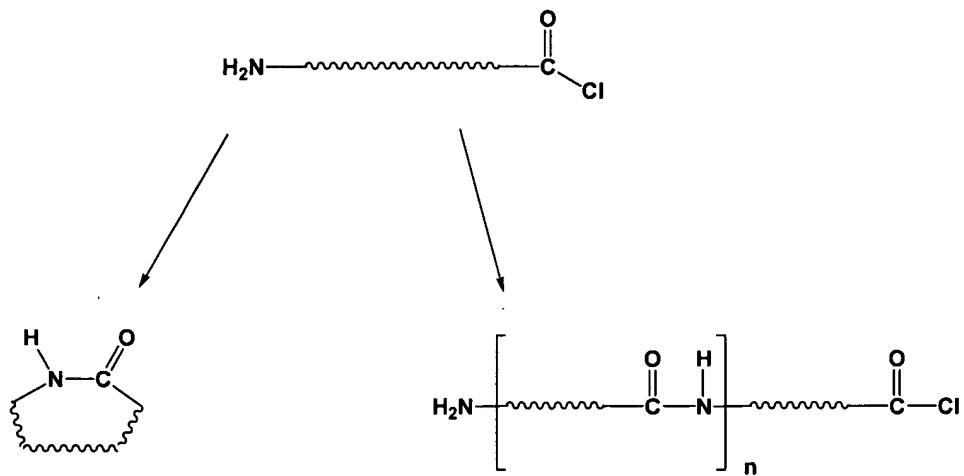
Claims 1-18 were rejected under 35 U.S.C. § 102(a) as allegedly anticipated over Han (U.S. Patent Application Publication No. 2002/0155999).

This rejection is respectfully traversed, as the Han reference has the following shortcomings. The Han reference fails to disclose how at least one of the porphyrin classes which it mentions can be linked with a chemotherapeutic agent. Etioporphyrin-I (referred to in Han as “etioporphin-I” at page 2, paragraph 25) has the following structure:



Han gives no indication as to how to link chemotherapeutic agents to etioporphyrins. In contrast, the instant Applicants' disclosure provides methods for derivatizing etioporphyrins, as is discussed above in the section dealing with the Rejection Under 35 USC § 112, First Paragraph.

Another shortcoming of the Han disclosure occurs in Figure 1. The lower scheme in Figure 1 apparently depicts the use of a linker compound having an amino group and an acid chloride. As depicted in Han, however, the chemistry could give a wide range of products. A compound with both an activated acyl group and an unprotected amino group could result in side reactions such as intramolecular reaction of the amino group with the activated acyl group (forming an unreactive cyclic compound), and intermolecular polymerization of the linker. These side reactions are depicted in the diagram below, where the wavy line is the portion indicated as the "Linker" in Figure 1 of Han.



In view of these shortcomings of the Han reference, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicants petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 578562000900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

By 
Robert K. Cerpa
Registration No.: 39,933
MORRISON & FOERSTER LLP
755 Page Mill Road
Palo Alto, California 94304-1018
(650) 813-5715